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Conradi, Henk Jan; Ormel, Johan; de Jonge, Peter

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Research Article

SYMPTOM PROFILES OF DSM-IV-DEFINED REMISSION, RECOVERY, RELAPSE, AND RECURRENCE OF DEPRESSION: THE ROLE OF THE CORE SYMPTOMS

Henk Jan Conradi, Ph.D.,[1,2]* Johan Ormel, Ph.D.,[2] and Peter de Jonge, Ph.D. [2]

Background: *Depression outcomes in research and clinical practice are commonly defined by the concepts of remission, recovery, relapse, and recurrence. Despite their widespread use, there has been little empirical examination of these concepts. Therefore, we investigated profiles of individual symptoms during each of these phases of depression.* **Methods:** *In a 3-year prospective study of 267 depressed primary care patients, we established the presence or absence of the individual DSM-IV depressive symptoms week-by-week during DSM-IV-defined remissions, recoveries, relapses, and recurrences. We measured symptoms in 12 quarterly assessments using the Composite International Diagnostic Interview.* **Results:** *Remissions were characterized by double the proportion of time that the core symptoms were present compared to the initial phase of recoveries after a major depressive episode (MDE; 59 versus 32%; Z = –3.03; P = .002). Before a relapse, remissions again showed elevated levels of core symptoms in comparison to the final phase of recoveries before a recurrence (58 versus 26%; Z = –2.99; P = .003).* **Conclusions:** *Compared with the initial and final phases of recoveries, remissions showed a consistently higher level of core symptoms. Clinically, this means that unresolved core symptoms in the direct aftermath of a MDE seem to constitute a risk for relapse and should be the target of preventive or augmented interventions. Depression and Anxiety 29:638–645, 2012.*

Key words: *DSM-IV; remission; recovery; relapse; recurrence; depression; symptom profiles; core symptoms; prospective study*

INTRODUCTION

In numerous treatment and observational studies that have been conducted over the past decades, the course of depressive disorders has been commonly described using the terms remission, recovery, relapse, and recurrence. A conservative search of Pubmed revealed over 1,000 articles concerning depression studies that used one or more of these terms in the title alone. Though these constructs are widely referenced in scientific research and clinical practice, they have rarely been empirically evaluated.[1]

In the late 1980s, inconsistencies in the application of these four constructs[2] led a task force to develop definitions and operational criteria for the terms based on observable phenomena.[3] Their definitions assumed the constructs would reflect temporal symptom changes over the patient's lifetime,[1] or qualitative change points that mark transitions in duration and severity of depression symptoms over time. Such transitions were assumed to be indicative of discontinuities in the course of the depressive illness.[2,3] One crucial distinction is that

[1]Department of Clinical Psychology, University of Amsterdam, The Netherlands
[2]ICPE (Interdisciplinary Center for Psychiatric Epidemiology), Department of Psychiatry, University Medical Center Groningen/University of Groningen, The Netherlands

*Correspondence to: Henk Jan Conradi, Department of Clinical Psychology, University of Amsterdam, The Netherlands. E-mail: h.j.conradi@uva.nl
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between remission and recovery. Remission is defined as a short period in which the patient has remitted from the preceding major depressive episode (MDE). However, remissions are rather unstable and are, by definition, quickly followed by a relapse, defined as a *revival* of the MDE preceding the remission. Recovery, however, is defined as a long lasting and, therefore, intrinsically more stable variant of remission. Recovery may be lifelong or followed by a recurrence. Recurrence is defined as the development of a *new* MDE after recovery has ended.[2,3]

In order to define each of the concepts, several propositions (depending on the assessment instrument used) were made regarding (1) *severity* criteria, or the number of symptoms present, and (2) *duration* criteria of symptom improvement as in remissions or recoveries, or deterioration as in relapses and recurrences. As stated by the task force,[3] these definitions are not evidence based and should be viewed as hypotheses in need of empirical study. To date, only two studies[4,5] have empirically investigated the constructs. These studies focused on the distinction between remission and recovery. They examined various time points at which ongoing remissions become defined as recoveries in terms of their prognostic value for the course of depression. Thus, they sought to determine the length of remission after which there is a marked decrease of the risk of the development of a subsequent MDE.

In this study, we did not examine different duration criteria for remission and recovery, but instead explored remission and recovery as defined by the DSM-IV duration criteria: <2 months not meeting criteria for MDE for remission and ≥ 2 months for recovery. We chose the DSM-IV duration criteria because it is the most widely applied diagnostic system. Furthermore, we did not focus on the patient's future course as a validator for remission and recovery, but instead investigated the internal structure of remission, recovery, relapse, and recurrence in terms of their constituting individual symptoms. We did this for two reasons. First, we are unaware of studies profiling individual symptoms in each of the four phases. Nevertheless, this is a basic question because symptoms are the building blocks of remission, recovery, relapse, and recurrence. Second, we wanted to know more about whether these four phases show different symptom profiles that might indicate symptom change or discontinuity over the depressive course. As mentioned before, symptom change underlies the definition of these four constructs. Consistent findings that residual symptoms during remission and recovery are important risk factors for relapse and recurrence further support our focus on symptoms.[6–8]

To bolster this symptoms-based approach, we established a framework by which to evaluate our symptom data. First, we conducted a plain descriptive analysis of the four phases of depression in terms of their profiles of individual symptoms.

Second, we compared the presence of the individual symptoms between the whole periods of remissions and recoveries and between relapses and recurrences to get a global impression of symptom (dis-)continuity over the depressive course. Since recoveries are, by definition, periods of sustained remission we expected lower levels of residual symptoms compared to remissions.

Third, after comparing the four *entire* phases, we zoomed in at important qualitative change points in the depressive course. We examined both remissions which, by DSM-IV definition, are followed within 8 weeks by a MDE (relapse), and recoveries, which may be followed by a MDE (recurrence) after at least 8 weeks or any time point thereafter which can be years. Because of this variable duration of recoveries, we compared remissions with two critical subphases of recoveries (Fig. 1). First, we compared remissions with the *initial phase* of recovery, which happens in the direct aftermath of a MDE and is the start of a long period of presumed sustained improvement. As mentioned, residual symptoms often play a profound role in triggering subsequent MDEs. Therefore, we anticipated remissions to be characterized by *elevated* levels of residual symptoms compared with the initial phase of recoveries, since relapses will soon follow remissions, whereas recurrences, in the case of recoveries, will not (Comparison 1). Second, we compared remissions with the *final phase* of recovery, just before recurrence. We expected *comparable* levels of residual symptoms during remissions and the final phase of recoveries because, in both cases, a MDE (a relapse or recurrence) is pending (Comparison 2).

MATERIALS AND METHODS

SETTING, PATIENTS, AND INCLUSION CRITERIA

Patients participated in a 3-year randomized clinical trial in a primary care setting (INSTEL) evaluating the effects of four treatments.[9] We included patients suffering from a current or recent MDE, occurring in the past 12 weeks, who were referred by their General Practitioner (GP), were between 18–70 years old, and were not suffering from a life-threatening medical condition, psychotic or bipolar disorder, dementia, or alcohol or drug dependency. We also excluded patients who were pregnant or already receiving psychotherapy.

The trial consisted of four interventions: Usual Care by the GP (UC; $n = 72$), a Psycho-Education Prevention program (PEP; $n = 112$), and PEP plus either psychiatric consultation (PC + PEP; $n = 39$) or brief cognitive behavioral therapy (CBT + PEP; $n = 44$). The number of patients per intervention was unequal because we anticipated differences in treatment effects. CBT + PEP and PC + PEP were expected to have greater effect than PEP alone in comparison to UC. UC, given by the GP, consisted of brief supportive counseling, possible antidepressant prescription, and/or referral according to clinical guidelines. PEP was a low-intensity program consisting of three face-to-face sessions and short quarterly telephone contacts thereafter. In the PC + PEP condition, one session with a psychiatrist preceded PEP, whereas in CBT + PEP on average 10 sessions of CBT were provided prior to PEP.

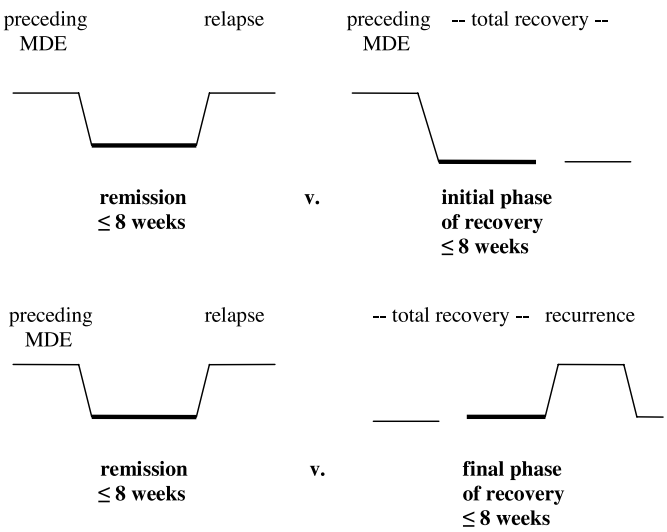

Figure 1. Comparisons between specific phases of depression (bold).
Comparison 1 (aftermath): In the aftermath of a MDE, remissions will have elevated symptom levels compared to the initial phase of recoveries.
Comparison 2 (prelude): During the prelude to an oncoming MDE, remissions, and the final phase of recoveries will have comparably elevated symptom levels

INSTRUMENT

At baseline, we administered the lifetime version of the *Composite International Diagnostic Interview* (CIDI) face-to-face. The CIDI[10,11] is a structured psychiatric interview that has shown good reliability and validity.[12,13] After baseline, patients participated in quarterly telephone interviews, which included an adapted CIDI depression section. We established the presence of each of the individual DSM-IV criteria, or symptom clusters, of depression during each week in the previous three months. Item parcels were created by counting the symptom group as present if any one of the symptoms that form the DSM-IV criterion were present. These symptom clusters include the two core symptoms of depression, depressed mood (feeling sad or empty), and/or diminished interest (or pleasure in activities), and the seven other symptom clusters: eating problems (weight gain or loss, and/or changes in appetite); sleeping problems (insomnia or hypersomnia); psychomotor problems (psychomotor agitation or retardation); fatigue or loss of energy; feelings of worthlessness and/or guilt (beyond mere self-reproach or guilt about being depressed); cognitive problems (diminished ability to think or concentrate and/or indecisiveness); and death ideations (recurrent thoughts of death and suicide). Based on this data on the week-by-week presence of individual symptoms, we were able to establish whether or not patients met criteria for DSM-IV-defined remission, relapse, recovery, and recurrence during each week of the follow-up period.

The interviewers who administered the quarterly telephone interviews were trained extensively by two supervisors who had been trained at the official WHO-CIDI Training and Reference Center at the Academic Medical Center in Amsterdam. Interviewers were supervised around once every 3 months. In order to support recall of individual symptoms over the preceding 3 months, interviewers provided respondents with their record of symptoms at the moment of the previous interview, that is, at the start of the previous 3 months. Subsequently, respondents were asked whether each symptom present had persisted the whole 3 months and, if not, how many weeks ago it resolved. If the symptom was not present at the start, respondents were asked whether it remained absent the whole 3 months and, if not, how many weeks ago the symptom developed, whether it persisted and, if not, when it resolved.

OUTCOME MEASURES

We defined the concepts of remission, relapse, recovery, and recurrence in accordance with the consensus paper[3] combined with severity and duration criteria from the DSM-IV. Thus MDEs, relapses and recurrences, were defined as two or more consecutive weeks in which the patient suffered from at least five out of nine DSM-IV-defined depressive symptoms, including at least one of the core symptoms. In the DSM-IV, a time frame of 2 months is applied as demarcation between a single episode of depression and recurrent depression. The latter refers to two distinct MDEs that are by definition separated by recovery. Remission was therefore defined as between two to eight consecutive weeks without a MDE, and relapse as a MDE that started *within* remission. Recovery was defined as at least 8 consecutive weeks without a MDE, and recurrence as a MDE that started *within* recovery. Remissions and recoveries may be partial, with patients suffering from residual symptoms.

During every phase, we computed the duration of the presence of each DSM-IV symptom cluster that patients reported. The proportions of time during which patients met the criteria for each symptom were added to compute a measure for the overall severity in each phase.

STATISTICAL ANALYSES

First, symptom profiles of the four phases were determined by calculating the proportion of time that each of the symptoms was present.

Second, we compared durations of individual symptoms between remissions and recoveries, and between relapses and recurrences, using Mann–Whitney nonparametric unrelated-samples tests. To determine the comparability of the symptom profiles, we computed Spearman's ρ nonparametric correlation coefficients between the rank order of symptom durations between remissions and recoveries, and between relapses and recurrences.

We used the same type of analyses for both the a priori Comparisons 1 and 2. We applied Mann–Whitney nonparametric two-related-samples tests *within* groups of patients. This enabled us to compare durations of symptoms during remissions and the initial and final phases of recoveries in the same patients. To make unbiased comparisons, we compared a patient's remission to the initial and final phases of recovery curtailed to the same duration as the remission. For example, if a patient reported a remission of 5 weeks followed by a relapse, we compared the remission to the initial and final 5 week period of recovery for that patient. Again, we computed Spearman's ρ nonparametric correlation coefficients between rank order of symptoms during remission and the initial and final phases of recovery. To correct for multiple testing, we set the significance level for all analyses at $P < .01$ (two tailed).

Finally, we performed sensitivity analyses to rule out possible treatment effects that could explain our findings. In the original study,[9] no differences were found between treatments during a 3-year follow-up on any of the CIDI-based outcomes, which was the measure of interest in this study. However, a relatively small difference emerged on the Beck Depression Inventory (BDI) between UC and PEP compared to PC + PEP and CBT + PEP. Therefore, we also conducted comparisons within both these subgroups separately. We combined UC with PEP, and PC + PEP with CBT + PEP and compared whether the findings in these subgroups corresponded with those from the whole sample.

RESULTS

PATIENT CHARACTERISTICS AND NONRESPONSE AT ASSESSMENTS

Table 1 shows sociodemographic and clinical characteristics of the sample. At baseline, there were no differences between treatment groups on these characteristics, apart from the finding that significantly more UC patients were married than CBT + PEP patients ($F = 8.08$; $P = .04$), and somewhat more UC patients reported severe depression at baseline compared to PEP patients ($F = 7.76$; $P = .02$). Nonresponse for the 12 quarterly telephone interviews ranged from 8.9% to on average 20%. Loss to follow-up was not associated with patient characteristics at baseline. See the original study for further details.[9]

TABLE 1. Sociodemographic and clinical characteristics at baseline

	$n = 267$
Mean age (*SD*)	42.8 yrs (11.3)
Female	65.0%
Education	
Low	43.8%
Middle	36.3%
High	19.9%
Marital status	
Married/cohabiting	64.8%
Not married	19.1%
Divorced	12.7%
Widowed	3.4%
Primary occupation	
Employed	60.3%
Homemaker	19.1%
Other	20.6%
Severity of index episode (DSM-IV)	
Mild	30.3%
Moderate	31.8%
Severe	37.9%
Recurrent episode (DSM-IV)	67.2%
>3 previous episodes (DSM-IV)	36.8%
Antidepressant medication	74.2%
Comorbid anxiety disorder (DSM-IV)	37.8%

ALL PERIODS OF REMISSION, RECOVERY, RELAPSE, AND RECURRENCE

Table 2 shows the proportions of time that individual symptoms were present during all combined periods of remission ($n = 88$), recovery ($n = 230$), relapse ($n = 55$), and recurrence ($n = 126$). Apart from the core symptoms, the longest lasting were cognitive problems, sleeping problems, and lack of energy, followed by feelings of worthlessness/guilt and eating problems. The least prevalent symptoms were recurrent thoughts of death and psychomotor problems. The mean durations of relapses and recurrences were comparable (11 and 14 weeks, respectively), whereas recoveries lasted far longer than remissions (67 and 4 weeks, respectively).

Next, we used Mann–Whitney nonparametric tests to compare the durations of individual symptoms and that of all symptoms combined, between relapses and recurrences. This revealed one statistically significant difference, namely on psychomotor problems (46 versus 26%; $Z = -2.96$; $P = .003$). The Spearman's ρ correlation coefficient between the rank order of individual symptoms during relapses and recurrences was 1.00 ($P < .001$).

Comparisons between remissions and recoveries revealed differences on the core symptoms (53 versus 15%; $Z = -3.97$; $P < .001$), cognitive problems (60 versus 41%; $Z = -2.75$; $P = .006$), death ideations (13 versus 10%; $Z = -2.73$; $P = .006$), and severity of overall symptomatology (3.33 versus 1.85; $Z = -7.83$; $P < .001$). The Spearman's ρ correlation coefficient between the rank order of individual symptoms during remissions and recoveries was .74 ($P < .04$).

REMISSIONS AND THE INITIAL AND FINAL PHASES OF RECOVERIES

First, we compared remissions with the *initial phase* of recoveries. We matched the length of the initial phase with that of the remission in the same patient (Comparison 1). Table 3 shows the durations of individual symptoms. The proportion of time that core symptoms were present was significantly greater during remissions than during the initial phase of recoveries (59 versus 32%; $Z = -3.03$; $P = .002$). Overall residual severity did not differ significantly. The Spearman's ρ correlation coefficient between the symptom rank order was .93 ($P = .01$).

Next, we compared remissions with the *final phase* of recoveries (Comparison 2). Again, we matched the period of the final phase of the recoveries to the duration of the patient's remission. Results (Table 4) reveal that

TABLE 2. Duration of presence of DSM-IV (residual) symptoms during remissions, recoveries, relapses, and recurrences

	Proportion of time that patients meet DSM-IV criteria per symptom cluster n = number of phases of depression; mean (SD); median (IQR)			
	Remissions $n = 88$	Recoveries $n = 230$	Relapses $n = 55$	Recurrences $n = 126$
Depressed mood/diminished interest	0.53 (0.48); 0.69 (0.00–1.00)	0.15 (0.22); 0.05 (0.00–0.21)	1.00 (0.00); 1.00 (1.00–1.00)	1.00 (0.00); 1.00 (1.00–1.00)
Cognitive problems	0.60 (0.47); 1.00 (0.00–1.00)	0.41 (0.36); 0.31 (0.09–0.73)	0.94 (0.23); 1.00 (1.00–1.00)	0.92 (0.22); 1.00 (1.00–1.00)
Lack of energy	0.49 (0.48); 0.36 (0.00–1.00)	0.32 (0.33); 0.18 (0.03–0.57)	0.89 (0.30); 1.00 (1.00–1.00)	0.85 (0.30); 1.00 (0.92–1.00)
Sleeping problems	0.53 (0.49); 0.93 (0.00–1.00)	0.35 (0.32); 0.26 (0.06–0.61)	0.82 (0.35); 1.00 (0.84–1.00)	0.80 (0.32); 1.00 (0.61–1.00)
Worthlessness/guilt	0.41 (0.47); 0.00 (0.00–1.00)	0.18 (0.27); 0.04 (0.00–0.29)	0.67 (0.45); 1.00 (0.00–1.00)	0.70 (0.39); 1.00 (0.39–1.00)
Eating problems	0.28 (0.42); 0.00 (0.00–0.60)	0.19 (0.26); 0.06 (0.00–0.33)	0.47 (0.45); 0.61 (0.00–1.00)	0.47 (0.43); 0.44 (0.00–0.98)
Psychomotor problems	0.20 (0.38); 0.00 (0.00–0.07)	0.12 (0.24); 0.00 (0.00–0.09)	0.26 (0.40); 0.00 (0.00–0.56)	0.46 (0.42); 0.47 (0.00–0.99)
Death ideations	0.13 (0.31); 0.00 (0.00–0.00)	0.10 (0.20); 0.00 (0.00–0.09)	0.24 (0.41); 0.00 (0.00–0.40)	0.33 (0.40); 0.00 (0.00–0.67)
Overall severity (range 0–9)	3.33 (1.40); 4.00 (2.38–4.00)	1.85 (1.29); 1.66 (0.76–2.79)	5.96 (0.94); 5.91 (5.00–6.60)	6.18 (0.86); 6.04 (5.50–6.78)
Duration (weeks)	3.92 (1.88); 3.33 (2.00–6.00)	67.15 (46.21); 56.75 (28.38–101.25)	11.00 (9.32); 8.00 (5.00–16.00)	14.01 (12.58); 10.00 (7.00–17.25)

the proportion of time that core symptoms were present during remissions was significantly greater than during the final phase of recoveries (58 versus 26%; $Z = -2.99$; $P = .003$), and that overall severity was higher (3.45 versus 2.67; $Z = -1.99$; $P = .006$). The Spearman's ρ correlation coefficient between the symptom rank order was .86 ($P = .007$).

DISCUSSION

This study is the first to examine the symptom profiles of remission, recovery, relapse, and recurrence. We found significant differences between remissions and recoveries, whereas relapses and recurrences resemble each other closely in duration and overall level of individual symptoms as well as the rank order of these symptoms. In the following, we discuss conceptual and clinical implications of these findings, after addressing limitations and strengths of the study.

LIMITATIONS AND STRENGTHS

One potential limitation to this study is that we did not differentiate between depressed mood and diminished interest. It may be interesting to examine whether one of the core symptoms is more responsible than the other for the difference found between remissions and recoveries. However, since both depressed mood and diminished interest refer to restricted motivation, we believe it is unlikely that this difference is decisive. Another limitation is that we did not examine interrater agreement on the presence or absence of symptoms. A final limitation may be that patients participated in a randomized controlled trial (RCT). Despite that, previously no differences were found between treatments on any of the CIDI-based outcomes.[9] Moreover, this study ruled out possible treatment effects by conducting sensitivity analyses. We tested whether treatment conditions (UC combined with PEP, and PC + PEP combined with CBT + PEP) were associated with the duration that individual symptoms were present. These tests showed no association.

An important strength of this study is its week-by-week assessment of individual symptoms by quarterly interviews over a 3-year follow-up. Compared with the earlier empirical studies of the four constructs,[4,5] our assessments were more regular. Also, rather than applying a cut-off based on depression severity scores,[4] we operationalized the four constructs, using the precise DSM-IV definitions based on presence/absence of individual depressive symptom clusters. With this we were able to make a novel contribution, namely insight into the structure of remissions, recoveries, relapses, and recurrences in terms of the percentage of time that individual symptoms are present. Furthermore, analyses in this study examined aspects of all four concepts, unlike the studies mentioned earlier.[4,5] Finally, we studied these constructs in a sample of depressed primary care patients. This has never been done before, though the

TABLE 3. Comparison 1 (aftermath): remission compared with the initial phase of recovery (matched on duration of remission) within groups of patients

	Mean (*SD*); median (IQR) proportion of time during remission and initial phase of recovery that patients meet DSM-IV criteria per discrete symptomcluster		Wilcoxon paired samples test *Z* (*P*)
	Remission ($n = 71$)	Initial phase recovery ($n = 71$)	Remission versus initial phase recovery
Depressed mood/diminished interest	0.59 (0.49); 1.00 (0.00–1.00)	0.32 (0.46); 0.00 (0.00–1.00)	**−3.03 (0.002)**
Cognitive problems	0.62 (0.47); 1.00 (0.00–1.00)	0.68 (0.46); 1.00 (0.00–1.00)	−1.11 (0.27)
Lack of energy	0.50 (0.49); 0.33 (0.00–1.00)	0.54 (0.49); 1.00 (0.00–1.00)	−0.43 (0.67)
Sleeping problems	0.49 (0.49); 0.33 (0.00–1.00)	0.53 (0.49); 1.00 (0.00–1.00)	−0.67 (0.51)
Worthlessness/guilt	0.40 (0.49); 0.00 (0.00–1.00)	0.31 (0.45); 0.00 (0.00–1.00)	−1.30 (0.19)
Eating problems	0.25 (0.41); 0.00 (0.00–0.50)	0.29 (0.45); 0.00 (0.00–1.00)	−0.71 (0.48)
Psychomotor problems	0.18 (0.38); 0.00 (0.00–0.00)	0.16 (0.36); 0.00 (0.00–0.00)	−0.46 (0.65)
Death ideations	0.11 (0.32); 0.00 (0.00–0.00)	0.14 (0.32); 0.00 (0.00–0.00)	−0.68 (0.50)
Overall severity (range 0–9)	3.33 (1.40); 4.00 (3.00–4.00)	3.09 (1.51); 4.00 (2.00–4.00)	−1.04 (0.30)

Note: bold signifies a statistically significant difference.

vast majority of depressed patients are treated in primary care.[14]

CONCEPTUAL IMPLICATIONS

As expected, the comparison between remissions and the full periods of recoveries revealed a significantly lower level of combined symptoms (3.33 versus 1.85). This was due to differences in the presence of the core symptoms (53 versus 15%), cognitive problems (60 versus 41%), and death ideations (13 versus 10%). This validates the conceptual idea of DSM-IV-defined recovery as a sustained period of improvement, whereas DSM-IV-defined remission is less stable, with considerable residual symptoms. Furthermore, recoveries were found to last much longer than remissions (67 versus 4 weeks, respectively). Recognizing that five or more symptoms constitute a MDE, we can consider remissions, with an average of 3.33 symptoms, as an intermediate period of subthreshold depression between the preceding MDE and the subsequent relapse. In other words, this may mean that partial remissions mark ongoing MDEs that are only temporarily subthreshold.

This difference between remissions and recoveries appears immediately after the preceding MDE has resolved, as suggested by comparing remissions and the initial phase of recoveries (Comparison 1). This seems due to a doubled duration of core symptoms during remissions compared to the initial phase of recoveries. The lower presence of the core symptoms during the initial phase of recoveries may indicate more stable improvement, which accords with the concept of recovery and suggests a qualitative change point in the aftermath of a MDE.

However, the comparison between remissions and the final phase of recoveries (Comparison 2) resulted in an unexpected finding. Based on earlier findings that residual symptoms are important triggers of MDEs, we expected remissions and the final phase of recoveries to show comparable (i.e., elevated) levels of residual symptoms since, in both cases, a MDE is pending. However, we found lower levels of all symptoms combined, and of the core symptoms in particular, during the final phase of recoveries. Our results seem to suggest that recurrences and relapses do not develop identically. Relapses, following remissions, may be seen as a development of residual symptoms that are unresolved during remission. Recurrences, on the contrary, seem to develop more unexpectedly, since the level of symptoms was significantly lower during the final phase of recoveries than during remissions (2.67 versus 3.45). It might be that recurrences are more suddenly triggered by new stressful events instead of a build up of dormant symptoms, as seems to be the case with relapses.

Taken together, DSM-IV-defined recoveries seem to be different from remissions as indicated by (1) differences in symptom ranking, and (2) lower levels of residual symptoms in general and of core symptoms in particular. These differences are evident immediately

TABLE 4. Comparison 2 (prelude): remission compared with the final phase of recovery (matched on duration of remission) within groups of patients

	Mean (*SD*); median (IQR) proportion of time during remission and final phase of recovery that patients meet DSM- IV criteria per discrete symptomcluster		Wilcoxon paired samples test *Z* (*P*)
	Remission ($n = 42$)	Final phase recovery ($n = 42$)	Remission versus final phase recovery
Depressed mood/diminished interest	0.58 (0.50); 1.00 (0.00–1.00)	0.26 (0.43); 0.00 (0.00–0.81)	**−2.99 (0.003)**
Cognitive problems	0.64 (0.48); 1.00 (0.00–1.00)	0.69 (0.46); 1.00 (0.00–1.00)	−0.50 (0.62)
Lack of energy	0.49 (0.50); 0.25 (0.00–1.00)	0.44 (0.50); 0.00 (0.00–1.00)	−0.52 (0.60)
Sleeping problems	0.48 (0.50); 0.17 (0.00–1.00)	0.40 (0.47); 0.00 (0.00–1.00)	−0.90 (0.37)
Worthlessness/guilt	0.41 (0.49); 0.00 (0.00–1.00)	0.38 (0.48); 0.00 (0.00–1.00)	−0.37 (0.72)
Eating problems	0.35 (0.45); 0.00 (0.00–1.00)	0.18 (0.37); 0.00 (0.00–0.00)	−1.78 (0.08)
Psychomotor problems	0.23 (0.42); 0.00 (0.00–0.00)	0.16 (0.36); 0.00 (0.00–0.00)	−1.03 (0.31)
Death ideations	0.14 (0.35); 0.00 (0.00–0.00)	0.12 (0.31); 0.00 (0.00–0.00)	−0.34 (0.73)
Overall severity (range 0–9)	3.45 (1.27); 4.00 (3.00–4.00)	2.67 (1.51); 2.79 (1.75–4.00)	**−2.77 (0.006)**

Note: bold signifies a statistically significant difference.

in the aftermath of a MDE. Thus, stability comes quickly in case of recoveries, suggesting a qualitative change point. Furthermore, the differences remain during the final phase of the recovery, suggesting different triggers for the oncoming MDE.

It should be noted that since the operationalization of remission and recovery by the task force, different definitions, based on the severity of symptoms, have appeared in the literature.[15] Our study was not able to validate these different definitions against each other, and we recommend this as a subject for future research.

We found no differences in symptom duration between DSM-IV-defined episodes of relapse and recurrence. Only psychomotor problems seemed to be more prevalent during recurrences (46 versus 26%); a finding for which we do not have an explanation other than chance. Despite this difference, symptom rankings were identical. This may suggest that, from the perspective of symptom profiles, the concepts of relapse and recurrence are interchangeable. The distinction between relapses and recurrences remains meaningful in the broader conceptual framework since they are each associated with different subthreshold phases in the course of depression, that is, remissions and recoveries, respectively.

CLINICAL IMPLICATIONS

Because residual symptoms are often found to be important predictors of MDEs,[6–8] it is highly relevant that we were able to identify the core symptoms in particular, as residual symptoms of interest in predicting relapses. Both depressed mood and diminished interest may refer to limited motivation of the patient as causal or maintenance factor. This may mean that remitted patients suffering from depressed mood and/or diminished interest have difficulty staying active, which may support the development of other depressive symptoms. This, in turn, may increase the risk of rapidly developing full-blown depression, more so than in patients with normal mood. Clinicians should view the presence of one or both of the core symptoms in patients who are subsyndromal as alarming, and make this the primary focus of preventive intervention.

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